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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
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EXAMINER

18N2/0127

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ART UNIT	PAPER NUMBER
1812	24

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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 16 December 1996

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) ~~1-34~~ 1, 3-5, 8-16, 18-20, 23-32, 34 is/are pending in the application.
Of the above, claim(s) 4-5, 10-11, 14, 19-20, 25-26, 29, 34 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 1, 3, 8-9, 12-13, 15-16, 18, 23-24, 27-28, 30-32 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☒ Claim(s) 1, 3-5, 8-16, 18-20, 23-32, 34 are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

DETAILED ACTION

Response to Amendment

1. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

2. The terminal disclaimer filed on 16 December 1996 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. Pat. No. 5,545,619 has been reviewed and is accepted. The terminal disclaimer has been recorded.

3. Claims 8-9 and 23-24 have been examined and are free of the prior art. There are no claims that are generic to these species. However, as indicated in Paper No. 21, page 4, subject matter that was examined in Paper No. 8 will be rejoined and examined with claims 8-9 and 23-24. In that Office action, a species election of an analog containing SCR domains from a different RCA protein was elected with a further election being that the species analog protein is CR1 (Paper No. 8, page 4). Claims 1, 3, 12-13, 15-16, 18, 27-28 and 30-32 are generic and will be examined only insofar as they read on an analog of CR1 containing SCR domains from a different protein. There are no species claims. Claims 4-5, 10-11, 14, 19-20, 25-26, 29 and 34 are withdrawn from further consideration by the Examiner, 37 C.F.R. 1.142(b), as being drawn to non-elected species.

Claim Rejections - 35 USC § 112

4. Claims 13 and 28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making a complement regulating protein analog containing

SCRs from a different complement regulating protein to confer C3b or C4b binding, does not reasonably provide enablement for making a complement regulating protein analog containing SCRs from a different complement regulating protein to confer decay accelerating activity upon the analog. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 13 and 28 recite a chimeric analog which has C3b, C4b and decay accelerating activity. The specification and prior art teach which SCR domains of the RCA proteins bind C3b and C4b. The specification and prior art also teach that DAF, CR1, C4bp and Factor H have decay accelerating activity and further teach that SCRs 2-4 of DAF are responsible for its decay accelerating activity (pp. 3-5). However, neither the specification nor the prior art teach which SCRs of CR1, C4bp and Factor H have decay accelerating activity. It was known in the art at the time the invention was made that the SCRs from different RCAs exhibit a high degree of sequence similarity, but that some combinations of SCRs mediate C4b binding, others mediate C3b binding, while others mediate decay accelerating or cofactor activity. Since the specification has not taught what the critical features of SCRs 2-4 from DAF are that confer decay accelerating activity and since the SCRs have a high degree of sequence identity but mediate different binding, decay accelerating or cofactor activities, it is unpredictable which SCRs from CR1, C4bp and Factor H would have the required decay accelerating activity. Absent guidance from the specification as to which SCRs of C4bp, Factor H and CR1 have decay accelerating activity, and given the lack of

predictability in the art, it would require undue experimentation for the skilled artisan to make protein analogs which have decay accelerating activity because he would have no reasonable expectation of success that adding any SCR or combination of SCRs from C4bp, Factor H or CR1 would result in an analog with the desired characteristic.

5. Claims 1, 8-9, 13, 16, 18, 23-24, 27-28, 30 and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 8-9 and 23-24 are rejected with respect to the recitation in the claims of substituting "structurally similar amino acids." Although the specification states that structurally similar amino acids include (I, L, V), (F, Y), (K, R), (Q, N), (D, E) and (G, A) (p. 15), the specification does not limit the definition to only these amino acid groups. Since all amino acids have the same carbon backbone, all can be considered to be structurally similar to one another. Furthermore, even if it is only the R group of the amino acid which is intended to be compared for structural similarity, the term is still unclear because "structural similarity" could mean that the R group had the same number of carbons, such that Leu, Glu and Gln all would be structurally similar to one another since each have a 3 carbon backbone, or it could mean that "structurally similar" amino acids have a similar charge, similar hydrophilicity, or a similar molecular size. Therefore, the term "structurally similar amino acids" is vague and indefinite because one cannot determine the metes and bounds of the claims as currently recited.

Claims 1, 8-9, 16 and 23-24 are indefinite for being in improper Markush format. Please see 2173.05(h) in the Manual of Patent Examining Procedure, revised 1 September 1995 for proper format. Removal of "and" after C4 binding protein in all claims and adding the term "consisting" after the first instance of "group" in claim 1 would overcome this objection.

Claims 8-9 and 23-24 are indefinite because "these complement regulating proteins" lacks antecedent basis. Removal of "complement regulating" would overcome this objection.

Claims 13 and 28 are indefinite because it not clear whether the unmodified protein or the protein analog has the required binding activities.

Claim 16 is indefinite because it is unclear whether what is being produced recombinantly by the method is an unmodified protein with its native sequence or a protein analog. Adding the term "analog" as the last word of the claim would overcome this objection.

Claims 18 and 28 are unclear because it is not clear what "protein" is being referred to.

Claims 23-24 are indefinite because they recite a method but do not recite any method steps. Adding the phrase "which method comprises expressing a DNA encoding the protein analog in a suitable host cell and recovering the protein analog" would overcome this objection.

Claims 23-24 are indefinite because the "protein analog" lacks antecedent basis. Adding the word "analog" after the first instance of protein would overcome this rejection.

Claim 27 is indefinite because it is unclear how "inserting into the protein analog" is to be accomplished by the method recited.

Claim 30 is indefinite because it is unclear whether the pharmaceutical carrier is to be added to the recombinantly produced protein or whether it is to be included in the method of making the analog.

Claim 32 is indefinite because "the host cell" lacks antecedent basis.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1, 3, 12, 15-16, 18, 27 and 30-32 rejected under 35 U.S.C. 102(b) as being anticipated by Lowell et al. (J. Exp. Med. 1989, 170, 1931-1946).

Lowell teaches chimeric CR1/CR2 protein analogs including one in which the first two SCRs of CR2 are substituted for the first two SCRs of CR1 (CR2/CR1 XE) (see Fig. 1, p. 1936 and p. 1939). Although Lowell does not disclose that this chimeric protein binds either C3b or C4b, as recited in the claims, it was known in the prior art that the first two SCRs of CR1 are required for C4b binding while SCRs 8-9 (and possibly SCR 10) and SCRs 15-16 (and possibly SCR 17) constitute two C3b binding sites (see p. 5 of specification and Klickstein, 1988). Thus, CR2/CR1 XE would have the property of binding C3b and would not be able to bind C4b, absent evidence to the contrary, as recited in claims 1, 3, and 12. In addition, Lowell teaches a method to express the analog recombinantly which includes construction of DNA encoding the protein

analog, transfection into host cells, and expression of the analog (pp. 1933-1935), as recited in claims 16, 18, 27, and 31-32. Lowell also discloses that cells expressing the chimeric protein were incubated with PBSA, which constitutes a pharmaceutical carrier (p. 1935), as recited in claims 15 and 30.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 13 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lowell et al.

The teachings of Lowell are disclosed above. Lowell discloses a chimeric RCA analog containing C3b and C3dg binding activity and a method of making the analog, but does not disclose an RCA analog containing C3b, C4b and decay accelerating activity. However, it is admitted as prior art in the specification that full-length CR1 had all three activities (Table 1, p. 3). Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the chimeric protein taught by Lowell and make an RCA analog in which the two N-terminal SCRs of CR2 are linked to the entire soluble CR1, rather than have substitution of the two N-terminal SCRs of CR2 for the two N-terminal SCRs of CR1, in order to obtain a chimeric RCA molecule which could bind C3b, C4b and C3dg and have decay

accelerating and cofactor activity. One would be motivated to make this modification in order to have a molecule which could be used diagnostically to determine the presence of any one of the complement proteins, C3b, C4b or C3dg, or which could be used therapeutically to inhibit complement activation through binding of C3b, C4b, C3dg and through its decay accelerating and cofactor activities. One having ordinary skill in the art would have had a reasonable expectation that a chimeric protein containing the two N-terminal SCRs of CR2 linked to CR1 would have the recited activities because Lowell teaches that CR2/CR1 XE chimeric analog, which contains only two SCRs from CR2, retains the C3dg binding activity of native CR2, which suggests that the SCR domains from different RCA proteins retain their binding or enzymatic activities when combined with another RCA protein.

Conclusion

10. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Karen E. Brown at (703) 308-3667, fax number (703) 308-0294. The Examiner can normally be reached Mondays through Thursdays and alternate Fridays from 7:30 a.m. to 5:00 p.m.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Stephen Walsh, can be reached at (703) 308-2957.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group Receptionist at (703) 308-0196.

KEB
14 January 1997

Stephen Walsh
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SUPERVISORY PATENT EXAMINER
GROUP 1800